

EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)Before 1900

According to the Boston Medical and Surgical Journal (20: 112-113, 1839), within less than 20 years of the time of writing, a new disease had developed in the country almost exclusively confined to parish ministers, consisting of loss of tone in the vocal organs attended by a sense of fatigue in the muscular apparatus of the throat, and accompanied by a peculiar dryness and rigidity of the lining membrane of the larynx; all of these circumstances concurred to destroy the original character of the voice, and finally to incapacitate many from discharging their pastoral duties. Dr. Mauran offered the observation that, to his knowledge, those clergymen who used tobacco did not suffer from this condition, from which it was inferred that smoking or chewing kept up a secretion in the neighborhood of the glottis, favorable to the good condition and healthy action of the vocal box. In contrast to the clergy of olden times who smoked and chewed very universally, since the great temperance reformation commenced and tobacco had been anathematized, it was now extremely rare to find any of the newcomers into the ministry who would tolerate tobacco. Not unnaturally, these observations raised a storm of controversy, which follows in chronological order: Woodward (*ibid.*, pp. 172-173) stated that in his experience, quite a large number of those suffering from the condition were users of tobacco, and he implicated instead a modern practice of preaching in vestries and thickly crowded, close and warm rooms, and afterwards inhaling cold air while heated. Mauren (*ibid.*, pp. 203-208) defended his position; and N. H. Allen (*ibid.*, pp. 220-222) agreed in general with Woodward that tobacco was injurious to the voice. R. A. M. (*ibid.*, pp. 247-248) was not able to agree with Woodward as to the pernicious effects of tobacco, since so many use it and apparently enjoy good health. "Senex" (*ibid.*, pp. 248-251) presented cases to show that loss of voice, though more frequent within the last 20 years, was not unknown at a much earlier period, and that in one case, to his knowledge, tobacco was not a preventive. From his personal knowledge, Woodward (*ibid.*, pp. 263-266) listed 3 cases of loss of voice in smokers; and Mauren (*ibid.*, pp. 343-347) cited 3 cases in which the condition was cured either by the assumption or resumption of smoking. Bacon (*ibid.*, pp. 280-283; 402) concluded that the affection was caused by speaking, and the remedy was to cease to speak; in 3 cases of bronchitis in clergymen recently come to his attention, 1 habitually used tobacco, 1 took water while speaking, and 1 did neither. It was reported (*ibid.*, pp. 316-318) that impairment of voice among clergymen was very rare in the South, while the practice of using tobacco was almost universal, and several cases were cited in which cessation of the use of tobacco led to the appearance of severe throat symptoms, which were corrected when the use of tobacco was re-established.

Regarding the effect of smoking on the voice in ordinary individuals, Wright (1846) remarked: "Particularly have I observed the buccal membrane to become vascular, swollen, irritable, and prone to hemorrhage. I have never observed an exception to the fact that in smokers the voice has deepened in tone (I suppose from relaxation), or become hoarse or oppressed through excessive mucous secretion. Many an irritable nervous cough, without increased secretion from the tracheo-bronchial membrane, and many a cough dependent upon increased secretion, have I known to follow the frequent use of tobacco in smoking."

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Gibb (1863) stated that the fauces, pharynx, larynx, and trachea were much more frequently affected from excessive smoking than were the bronchi and mouth:

Stugocki (1867) described a case of tonsillitis attributed to pipe-smoking.

Stugocki (1867) attributed a case of laryngitis to smoking;

According to Ladreit de Lacharriere (1878), the angina of smokers is characterized by swelling, redness, dryness, and insensibility of the mucous membranes of the soft palate and of the pharynx. The swelling is uniformly distributed; it is particularly appreciable at the uvula, which presents a much larger volume and which is sometimes deviated slightly to either the right or left. The mucous membrane is not red, as in acute phlegmatic conditions, but is of a darker color; it is rather a congestive red than inflammatory. The dryness of the throat seems evident; the epithelium which covers the mucous membrane is glossy and brilliant. The patients show no pain, no sensitiveness, and invariably declare they have no sore throat; they demand care only after the subjective symptoms (buzzing and deafness) appear.

Rumbold (1880) considered that the local effect of tobacco on the mucous membrane of the nose, throat, and ears was predisposing to catarrhal disease through causing a more permanent relaxation and congestion than any known agent; and, in the presence of such changes, even slight exposure to cold results in catarrhal inflammation.

According to Rumbold (1880), the use of tobacco should be immediately discontinued by every catarrhal patient.

A writer who signed himself "M. D." (1885) reported a case of chronic pharyngitis kept up by excessive cigarette-smoking.

Coomes (1887) held that 95% of smokers have something abnormal or unhealthy about the upper air passages—pharyngitis, laryngitis, chronic irritation in the nose.

According to Bosworth (1889), pharyngeal or nasal catarrh should not be attributed to the use of tobacco; according to Mulhall (1895a, b, c), tobacco produces, at most, a slight hyperemia or insignificant catarrh in the healthy throat.

In many cases, an existing catarrhal condition may be aggravated by tobacco (Bosworth, 1889; Mulhall, 1895a, b, c).

Jankau (1894) recommended that smoking be stopped in all diseases of the larynx and pharynx.

C. C. Rice (1897) reported that constant contact of tobacco-smoke with the mucous membrane of the respiratory tract resulted in the development of inflammatory conditions in those disposed to disease of this portion of the body much earlier in life than would otherwise be the case. In his experience, smoking caused advanced atrophic nasal catarrh, with dryness and congestion of the pharynx.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)1900 - 1919

Langmaid (1904, 1905, 1943) claimed he could recognize the non-smoker by the appearance of the throat.

Langmaid (1904, 1905, 1943) believed that tobacco-smoking was not only harmful to the throat as a direct irritant, but that it produced vasomotor disturbances of the pharyngeal mucous membrane through its toxic effects upon the nervous system.

In Lack's (1905) experience, corroborated by careful inquiry among a large number of singers and other professional voice-users, the effects of tobacco-smoke on the throat were greatly exaggerated. Lack considered it safe to state that moderate smoking never originated any affection of the throat worthy of the name, causing at most a slight hyperemia of the parts with which the smoke comes in contact, or an insignificant catarrh; the slight huskiness of the voice ascribed to smoking will more often be found to depend upon alcoholism or dyspepsia than upon excessive smoking.

P. Steiner (1906) described 3 cases of cancer of the larynx; one of the patients used tobacco excessively.

After a review of the literature, Reik (1910) stated that there was not one scintilla of evidence that malignant disease of the throat was due in any way to the use of tobacco. Other writers, however, have maintained that tobacco can cause throat cancer (Abbe, 1916a; Lickint, 1930b); and Wynder (1956) considered the evidence as good that tobacco is a causative agent in cancer of the hypopharynx.

In a series of 136 cases of carcinoma of the pharynx, 33 patients designated themselves as heavy and very heavy smokers; 8 chewed tobacco (Schumacher, 1912).

With respect to tuberculosis of the larynx, Dworetzky (1918) stated that local irritants, such as tobacco, have a deleterious effect on the larynx, producing a catarrhal condition with consequent formation of a favorable site for the implantation of the tubercle bacillus; therefore, tobacco was contraindicated in tuberculous lesions of the larynx. Duboff (1918) studied 1,000 case-histories of 793 males, of whom 46.4% were smokers, and of 207 females, none of whom smoked. Among the males, throat tuberculosis was no more common among smokers than among non-smokers; among the females, the incidence of throat tuberculosis was as high as among the males, from which the author concluded that throat complications were no more frequent in tobacco-users than in those who use no tobacco, and that tobacco obviously did not predispose to laryngeal complications. In commenting upon this paper, The Lancet (i: 745, 1918) suggested that Duboff's argument was based on rather slender statistical evidence.

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1920 - 1929

Kelly (1921) directed attention to an uncommon variety of acute laryngitis characterized by the deposition of fibrin and the occasional formation of erosions of the vocal cords which he encountered in 40 soldiers during World War I; among the many predisposing causes of this condition, he instanced the overuse of tobacco.

Terbrüggen (1923), who considered the chief irritant in tobacco-smoke to be ammonia, stated that, if a patient with chronic catarrh could not stop smoking, one should recommend to him the cigarette, which produces less ammonia than the cigar, to be used in moderation without inhaling. Mentholated cigarettes were especially recommended.

W. M. Johnson (1929) stated that most inveterate smokers show some congestion of the pharynx, regardless of the brand of tobacco smoked;

W. M. Johnson (1929) was convinced, as a result of more than 3 years' clinical study, that the chief effect of tobacco-smoking was a local one exerted on the mucous membrane of the pharynx, less frequently on the larynx and trachea, and exceptionally on the bronchi.

Bogen (1929) found that 5% of smokers studied by him complained of hoarseness:

In Bogen's (1929) series of smokers, 30% reported coughing.

Of 33 cases of cancer of the fauces in his series, 32 (including 1 woman) were heavy pipe-smokers; and so constant was the association of prolonged smoking with this condition that Mowat (1929) was tempted to call it *the "smoker's cancer."*

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)1930 - 1939

Some writers have expressed the belief that tobacco-smoking is an etiological factor in the development of cancer of the larynx (Lickint, 1930b; Jackson and Jackson, 1939, 1941; Heermann, 1941; Wynder, 1952b, 1956; Wallner, 1954b; Blümlein, 1955, 1957).

F. L. Hoffman (1931) stated that cancer of the larynx had increased from 0.5 per 100,000 cancer deaths in 1915 to 0.9 in 1923, concomitant with an enormous increase in cigarette-smoking. But Orton, (1938) stated that no great increase of cancer of the larynx has followed promiscuous smoking of cigarettes by either men or women.

Hoffman (1931) reported that 13 of 26 patients with cancer of the tonsils were heavy smokers.

(of cancer of the larynx)
F. L.
Hoffman (1931) reported 37 cases, of whom 16 were heavy smokers; G. Tucker (1935), 200 cases, of whom 25 gave a history of excessive tobacco-use; Orton (1938), 102 cases, of whom 38 gave a history of excessive tobacco-use; Heermann (1941), 30 cases, of whom 26 were habitual heavy smokers; A. E. Hammond (1942), 15 cases, of whom 6 gave a history of excessive smoking.

Felderman (1931) also stated there was no conclusive evidence that tobacco was injurious to the throat, and added: "Not only is smoking a social habit but it is a substantial help to those who follow the profession of speaking or singing, for in both of these undertakings a certain amount of mental labor and concentration is required, whether in composing speeches or studying an operetta. Smoking is a much safer habit than over indulgence in foods."

Moratti (1932) pointed out that case-histories of patients with leukoplasmia, epithelioma of the mouth, carcinoma of the hypopharynx, esophagus, and stomach, almost always reveal an inveterate habit of smoking and chewing tobacco.

H. Farrell (1933) examined the nose, throat, and chests of 85 men and 15 women cigarette-smokers, and reported that "though slight, there may be seen and felt some changes of an inflammatory nature in the different tissues of the gums, buccal surface, tongue, tonsils, pharynx, larynx, trachea, and esophagus of the inveterate cigarette-smoker. However, this chronic catarrhal condition of the mucous membrane is seldom, if ever, provoking, and it is a rare occasion that the habitue calls on a specialist for relief of sore throat."

Pipe-smoke and cigar-smoke are not inhaled because of their harshness, and these, according to Thys (1935), lead to cancer of the buccal cavity; while, because it is less irritating, cigarette-smoke is deeply inhaled, and hence leads to pulmonary cancer in heavy cigarette-smokers.

G. Tucker (1935) considered that excessive use of tobacco was probably a predisposing cause of a number of his cases of cancer of the larynx;

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M. M. Kennaway and E. L. Kennaway (1936) examined the death certificates of cases of cancer of the lung and of the larynx in males from England and Wales for 1921-32; there were 8808 cases of lung cancer, and 9472 cases of laryngeal cancer. The incidence of lung cancer in tobacco manufacturers was found to be 196, of laryngeal cancer 65; the incidence of lung cancer in tobacconists and their assistants was 175, of cancer of the larynx 142. In interesting contradistinction, those occupied in supplying alcohol showed a much higher incidence of laryngeal than of lung cancer.

It has often been noted that cough is a constant sign in many heavy smokers, especially cigarette-smokers (C. C. Rice, 1897; Fantus, 1936; R. B. Scott, 1952a, b; Myerson, 1953; Joules, 1954; W. C. Boake, reported in *Lancet*, Lond. 1: 512, 1957; I. Gordon, 1957; among others).

According to Bogen (1937), it appears that smoking may lead to more frequent localization of tuberculosis involvement in the larynx. Statistical investigations were said to show a higher incidence of laryngeal lesions among tobacco-users, and clinicians repeatedly report that patients recover from this complication more readily if they abstain from smoking, although similar improvement is reported following the "silence" or laryngeal-rest treatment.

Ahlbom (1937) reported that tobacco was used by 86% of 312 male lip-cancer patients, while, in contrast, there was a 98% incidence of tobacco-use in 233 cases of the oral cavity, larynx, pharynx, and esophagus, as well as in 68 cases of buccal, gingival, and mandibular cancer. Of 132 women with cancer of the oral cavity, only 15% used tobacco; and among 113 women with cancer of the pharynx, larynx, or esophagus, tobacco appeared not to have played a role.

A number of observers have suggested, or found, that different modes of tobacco use are related to the development of cancer at one particular site. Of the 312 cases of lip cancer in men reported by Ahlbom (1937), 57% smoked pipes, 6% used cigars and cigarettes, 37% used snuff and chewing-tobacco (some obviously used more than one form). In contrast to this, of 233 male cases of cancer of the oral cavity, larynx, pharynx, and esophagus, 25% were pipe-smokers, 40% cigar- and cigarette-smokers, and 35% used snuff and chewing-tobacco. Of 68 cases of buccal, gingival, and mandibular cancer, 23% were pipe-smokers, 7% cigar- and cigarette-smokers and 70% used snuff and chewing-tobacco. Of 87 male cases of cancer of the pharynx, larynx, and esophagus, 20% used pipes, 64% cigars and cigarettes, and 16% snuff or chewing-tobacco.

In their book on the larynx and its diseases, Jackson and Jackson (1937, p. 378) presented this formulation of the cause of cancer:

$$A + S + C + I + F + a + T + H + xyz = E$$

where a = alcohol and T = tobacco.

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(of cough)

Jarvis (1938), on the other hand, considered the cause to be tobacco dust; he had cigarette dust counts made by a dust-count engineer, which enabled him to state that each time one inhales from a cigarette, one takes in 120,000 particles of dust 10 microns or under in size. Hence, smokers were said to present a mild dust problem, wherein dust might overload the lung lymphatics, and bring about cough. Application of the wet-filter principle (moistening of the mouth end of the cigarette with saliva for about one-fourth inch before lighting and starting to smoke it) was found to reduce the dust counts, develop a cool smoke, and result in disappearance of cigarette cough within 2 weeks in the majority of patients. Jarvis added: "If the cough does not markedly disappear in two weeks' time, one looks elsewhere for the source of the cough."

Hollis (1939) considered tobacco catarrh as a disease-entity which should be managed as such. He observed that in virtually all cases, the nasal membranes were less colored after smoking and the airways definitely more patent, and stated that a daily routine of these rapidly-changing phenomena repeated 20-40 times would, and undoubtedly did, cause chronic secretory changes, altered response of the mucous membranes to environmental changes, relaxation, and undue thickening of surface and sub-surface tissues, with shortness of breath, cough, and hoarseness. Three cases were presented in which laryngeal conditions cleared up upon abstinence from tobacco.

Hollis (1939)

felt very certain that very many Americans who are constantly "out of voice" were suffering from a low-grade chronic hypertrophic laryngitis resulting from a so-called tobacco cough.

Hollis (1939) was inclined to believe that tobacco played a definite part in the production of contact ulcer of the larynx. In some 10 cases of this condition seen by him in smokers, simple voluntary aphonia was not sufficient to effect a permanent cure, and withdrawal of tobacco was necessary in order to bring about reasonably prompt recovery. Perhaps on the basis of this work, avoidance of tobacco was recommended in the treatment of contact ulcer of the larynx (J. A. M. A. 128: 1259, 1945).

Jackson and Jackson (1939) considered it was the smoke, not the nicotine or the tobacco as it grows naturally, which constituted the irritative factor in the development of cancer of the larynx, and that it was the empyreumatic oil of tobacco produced in the destructive distillation of burning tobacco which was the essential irritating factor in tobacco-smoke.

Jackson and Jackson (1939) and Wallner (1954a, b) considered tobacco-smoke a large factor in the production of chronic laryngitis.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)1940 - 1949

In view of the relatively enormous increase in the use of smoking tobacco by women, and of the hitherto rare incidence of this disease in females, Jackson and Jackson (1941) remarked that it would be interesting to note the incidence of laryngeal cancer in women during the next decade.

Kaye (1942, 1944) reported that a high percentage of soldiers suffered from catarrh of the upper respiratory passages, and that this condition was aggravated by the excessive use of tobacco so prevalent in the army.

According to Podolsky (1943), "Oil in tobacco smoke is another suspected cause of" cancer of the throat.

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Fischer (1943) considered it had not been proven that smoking plays a part in cancer of the larynx;

Regarding the mechanism of smoker's cough, M. F. Jones (1943) considered the condition to be a result of the effect of nicotine on the autonomic nervous system, resulting in altered secretions of the nose, pharynx, trachea, and bronchi. Cigarettes have a greater effect than cigars or pipes because inhaling increases the contact with the mucous surface through which the nicotine is absorbed.

According to Kaye (1944), the limitation of smoking for even 2 or 3 days will exert a beneficial effect upon smoker's cough. M. F. Jones (1943) considered the best remedy to be 6 weeks without tobacco.

In a series of 167 cases of cancer of the larynx reported by Mustakallio (1944), all but 2 were smokers, and 45 out of 100 of these cases smoked at least a pack of cigarettes a day. According to Clerk, Putney and O'Keefe (1948), a majority of 369 patients with carcinoma of the larynx used tobacco either moderately or excessively.

Potter and Tully (1945) analyzed information on the use of tobacco obtained from 2927 male clinic patients over the age of 40 in Massachusetts, and concluded there was a definite association between cancer of the buccal cavity and the use of tobacco, and that there also appeared to be some association between the use of tobacco and cancer of the respiratory tract. Cancer of the digestive tract, cancer of the skin, and cancer of all other sites was not related to smoking.

A. E. Hammond (1942) considered that the use of tobacco appeared to be a prominent contributing factor in cancer of the larynx;

Clerk, Putney and O'Keefe (1948) stated that nothing was shown to substantiate the belief that smoking was a predisposing factor. *(for cancer of the larynx)*

Patients having smoker's cough usually show no abnormal physical signs in the chest (Gusterson, 1945)

a report by Heermann (1941) is interesting. This writer described the case of identical twins, in one of whom cancer of the vocal cords developed; and, since the one who developed cancer smoked, and the other did not, it was concluded that tobacco was the etiologic factor and, by inference, that a genetic predisposition was not present.

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Schnur (1946) recorded 5 cases of patients who were moderate to heavy smokers (more than 1½ packs of cigarettes daily) and who had been coughing from 0.5-8 years; generally, the cough was non-productive and was exacerbated at night and in the morning. It developed that the cough was due to the use of tooth-powder, and eliminating its use diminished markedly or eliminated the cough in each of these patients without other therapy. Schnur's explanation was that the irritation of smoking raised the sensitivity of the mucous membrane of the pharynx, so that the small particles of tooth-powder which adhered to the posterior pharynx acted as an excitant sufficient to initiate the cough reflex. Such action was not allergic, but due to the irritation of an insoluble foreign body upon a hypersensitive membrane. The cough was aggravated immediately after brushing the teeth in the morning and evening, and was diminished during the day as the particles of grit were mechanically removed from the pharynx.

According to Fabricant (1946b), evidence of chronic pharyngitis, chronic laryngitis, and chronic tracheitis, characterized by symptoms of a sensation of rawness, sore throat, occasional hoarseness, and the production of laryngotracheal secretions, is found either individually or collectively in smokers who abuse tobacco. Such individuals can become free of symptoms by stopping smoking for a period of 5 weeks; conversely, they can reproduce their complaints by resuming smoking. In a general way, abuse can be defined only as that amount of smoking which would produce distress in the smoker's throat. Patients should be told to smoke within moderation, moderation depending on what the throat tells the smoker.

R. S. Stevenson (1947), discussing the throat in relation to singing and public speaking, stated that tobacco caused harm to the larynx by its local, not (as in the case of alcohol) by its systemic effect, the harmful agents being not nicotine so much as the burning of the chemical products by the destructive distillation of the tobacco. He suggested to singers with voice trouble that he himself would not personally smoke if he were a professional voice-user. If smoking were indulged in, the first third only of a cigarette was preferable.

Following an analysis of death certificates for cancer of the lung and cancer of the larynx in males from England and Wales for the years 1921-1938 inclusively, E. L. Kennaway and N. M. Kennaway (1947) stated: "Among various possible factors which have been suggested to account for the increase is tobacco smoking: the consumption of tobacco has risen, and so has the percentage of it smoked in the form of cigarettes, of which the smoke is often inhaled; such an effect of tobacco would accord well with the absence of social gradient."

When the occupational distribution of 139 patients with endolaryngeal cancer was compared with the occupational distribution in the Netherlands (1920 census), a large proportion were found to work in the "immaterial" professions, and few in the agrarian professions (Wassink, 1948).

H. Martin (1948, 1949) felt that, although excessive smoking with inhaling might be one of the etiologic factors in an occasional case of laryngeal cancer, smoking could not be shown to have a significant etiologic role in most cases of the disease.

According to H. Martin (1949), the addiction to tobacco among male patients with cancer of the tonsils is almost 100%.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)1950 - 1959

Myerson (1950) described a localized lesion of the vocal cord attributed to excessive smoking, and reported having seen the lesion in various stages in 143 patients, most of whom smoked 40 or more cigarettes daily. Histologically, this lesion was one of localized edema which becomes chronic, and as a result of chronic edema, fibrous connective tissue forms in the stroma, and an edematous fibroma results. Treatment is surgical, except in the early stage, when the lesion is purely edematous.

In a series of 73 cases of cancer of the larynx and pharynx, Schrek and his associates (1950) found 69.9% cigarette-smokers, compared to 48.8% in a control group.

In a series of 73 cases of cancer of the larynx and pharynx, there were 69.9% cigarette-smokers, compared to 48.8% in a control group (Schrek *et al.*, 1950).

Moffett and McFarland (1950) pointed out that, in the past 10 years when more women had been smoking, and probably more of them drinking, there had not been any significant increase in incidence of laryngeal cancer in the female sex.

Moffett and McFarland (1950) considered that use of alcoholic beverages *per se* was not a significant etiologic factor of cancer.

G. Tucker (1935) and A. E. Hammond (1942) considered that vocal abuse appeared to be a predisposing or contributing cause in cancer of the larynx; but Moffett and McFarland (1950) thought not.

Moffett and McFarland (1950) considered that the etiology of the condition had not been established, but that smoking *per se* was not one of the significant etiologic factors of cancer. (cancer of larynx)

E. L. Kennaway and N. M. Kennaway (1951) also noted that, in spite of the increased consumption of tobacco, the incidence of laryngeal cancer in women had been stationary for the last 15 years, while the prevalence of cancer of the larynx in men appears to be decreasing.

Common experience, however, must recognize the existence of smoker's cough (R. B. Scott, 1952a, b), and many patients with this condition will get surprising relief on stopping smoking (Guerrant, 1951).

Grantham-Hill (1952) recorded having had a cigarette cough due to tracheitis, which disappeared after he began making and smoking his own cigarettes with rice paper.

R. B. Scott (1952a, b) stated that irritation from heavy smoking leads to chronic pharyngitis; but Myerson (1955b) remarked that the pharynx seems to be spared in a majority of smokers.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

A detailed account of smoking habits in 226 patients with malignant tumors of the larynx by Valko (1952) showed that 209 of 219 men smoked (188 were cigarette-smokers), while none of the 7 women in the series smoked. In a control group of 108 male patients of the same age-group with a diagnosis other than malignant tumor of the larynx, there were 77% smokers.

Deaths from lung cancer in males occurred in excess and at a relatively early age in England and Wales, compared to the United States; in contrast, deaths from cancer of the larynx and trachea occurred in excess and at a relatively early age in America (Hewitt and Brooksbank, 1952).

In a series of 125 cases of keratosis of the larynx studied by Putney and O'Keefe (1953), 11.2% were said to be non-smokers. . . , they felt this figure might be significant when compared to the finding of 34% non-smokers in the survey of Mills and Porter (1950).

Kirchner and Malkin (1953) reported that, in a series of 235 cases of cancer of the larynx observed at New Haven Hospital over 30 years, 100 (43%) were classified as smoking excessively (over 1 pack a day) or chewing to excess; the authors noted that many more "moderate" smokers were not included.

Of 13 patients with carcinoma of the larynx, 7 were heavy smokers, 4 smoked moderately, and 2 were non-smokers (A. H. Miller and Fisher, 1953).

Some information concerning the relatively frequency of cancers in the various laryngeal regions is given by Friedberg and Wallner (1953). Of 31 cases of cordal carcinoma, all but one gave a history of smoking, and two-thirds smoked in excess of 1 pack per day; 19 of these revealed evidence of leukoplakia, and the majority of these patients were excessive smokers (2 packs or more a day). Of 18 patients with endolaryngeal carcinoma, all but 4 had a history of smoking; information as to smoking habits was not available for the remainder. Of 9 patients with subglottic carcinoma, 6 gave a history of heavy smoking; no smoking information was available for the other 3. Of 58 patients with extra-cordal carcinoma, 47 were habitual smokers, 9 were moderate smokers, and 2 were non-smokers.

Sadowsky, Gilliam and Cornfield (1953) found what they considered to be a real statistical association between cigarette-smoking and laryngeal cancer; in a series of 1990 cases of cancer of the lip, tongue, other oral-cavity sites, pharynx, esophagus, larynx, and lung, smoking histories showed that 91.9% of the patients smoked, compared to a 86.8% incidence of smoking in a control group of 615 patients with illnesses other than cancer.

In their statistical studies on smoking and cancer already described, Sadowsky, Gilliam and Cornfield (1953) observed no statistical association between pharyngeal cancer and smoking of any type:

The only specific reference to unburned tobacco in relation to laryngeal cancer appears to be by Kirchner and Malkin (1953), who reported that an unspecified number of their laryngeal-cancer patients chewed to excess.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

The sex differential for laryngeal cancer was reported by Dorn (1953a) to be greater than that for cancer of the lung and bronchus, the ratio of male to female morbidity rates being 10.6, or twice as large as for lung cancer. Male-female ratios in cases of cancer of the larynx reported by various authors bear out the sex-linked character of this disease: 20.5:1 (Valko, 1952); 37.7:1 (Friedberg and Wallner, 1953); 24.5:1 (Fusari, 1957); 6.8:1 (Montreuil, 1956).

Doll (1954a) noted that cancer of the larynx had, in the past, provided a good example of a type of cancer which was closely dependent on social conditions; but that the increasing gradient with descent in the social scale revealed in 1921-1923 is, however, now no longer apparent.

Baltzell and Putney (1954) surveyed 1498 cases of cancer of the larynx seen in the bronchoscopic clinic of Jefferson Hospital, Philadelphia, during 1928-1953. Of these, 186 (12%) were non-smokers, a figure which the authors compared to the 34% non-smokers in the general male population of Columbus, Ohio, as reported by Mills and Porter (1950). Regarding the smoking histories of the smokers, 249 patients smoked less than 1 pack of cigarettes daily, 563 smoked 1-2 packs, 152 smoked 2-3 packs, and 39 smoked more than 3 packs daily; 55 patients were moderate smokers of pipe and/or cigars, 62 were excessive smokers of pipe and/or cigars, and 82 were excessive smokers of pipe, cigars, and cigarettes; the smoking history of 110 patients was unknown.

Baltzell and Putney (1954) stated that, although more smokers were found in their series than in the normal population, this did not necessarily incriminate tobacco as an etiologic agent.

In the bronchoscopic clinic of Jefferson Hospital, Philadelphia, 84 cases of cancer of the larynx were seen during 1928-1933, 450 during 1934-1943, and 964 during 1944-1953; whether this increase was real and absolute could not be definitely answered by Baltzell and Putney (1954).

In an analysis of mortality from cancer of the larynx in the County Boroughs, Urban Districts, and Rural Districts of different parts of England and Wales for 1946-1949, Curwen, Kennaway and Kennaway (1954) showed that the Standard Mortality Ratio for cancer of the larynx in males increased with increasing urbanization, while cancer of the female larynx showed exactly the reverse relationship. From an analysis of the anatomical and sex distribution of 964 cases of cancer of the larynx, it appeared that this condition in men and in women are to a large extent different diseases, the so-called extrinsic group being more frequent in women.

Wallner (1954b) wrote that, although the etiology of cancer remained an enigma, chronic irritation was frequently listed [e.g. by Baltzell and Putney (1954)] as an important factor; and if one accepts smoking as an etiologic factor in keratosis, one must also regard it as a factor in the development of cancer of the larynx, since precancerous lesions are said to be important in the development of laryngeal carcinoma.

The cough is more marked in the morning (Joules, 1954), increases progressively with increasing cigarette consumption (A. M. Phillips, R. W. Phillips and Thompson, 1956) and with age (Joules; Phillips *et al.*)

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

Ryan, McDonald and Devine (1955) compared microscopic sections from larynges from 3 non-smokers and 9 smokers, all of whom were men aged 40-60 years with no history of hoarseness or voice strain or recent complaints referable to the larynx, and who had died a relatively sudden death; they found (1) a thicker surface epithelium in smokers than in non-smokers, due in part to excess keratinization of the true cord, but mostly to epithelial hyperplasia at all three sites measured, namely, the false cord, the true cord, and the subglottic area; (2) a greater degree of round-cell infiltration in the smokers; (3) slightly more edema in the smokers; and (4) the presence of squamous-cell metaplasia in only the excessive smokers in this study. In a second study, a random series of 60 male subjects in the 40-60-year age-group was taken, and the foregoing criteria were used to designate the larynges as normal or not normal, "normal" being defined as the appearance of the larynx seen in the non-smoker in the pilot study. Smoking habits were ascertained following the study, and reliable information obtained on 40 of the cases. In 6 of 9 non-smokers, the epithelium was judged normal, while of 26 heavy or excessive smokers (16 or more cigarettes per day), 4 were judged to have normal-appearing epithelium. In the group of 5 light-to-moderate smokers, 3 were judged to have normal appearance, but 2 of these were cigar-smokers (who usually do not inhale). The authors concluded that this evidence supported the thesis that excessive smoking is associated with pathologic changes in the larynx.

In Blümlein's (1955) series of 241 cases of laryngeal cancer in males, 95.5% were heavy or very heavy smokers who habitually inhaled cigarette-smoke, and 87% had been cigarette-smokers for many years. In a control group of 200 cancer-free patients, heavy smokers amounted to only 9.3%; and there were 18% non-smokers compared to 0.8% non-smokers in the laryngeal-cancer group.

Blümlein (1955) maintained that there was a real increase in laryngeal cancer, and that the habit of cigarette-smoking alone could be held responsible for the increase in laryngeal cancer among the male sex. Other authorities, however, have noted that, in contrast to the increase in mortality due to cancer of the lung, the mortality due to cancer of the larynx has shown little change (Sadowsky, Gilliam and Cornfield, 1953; Curwen, Kennaway and Kennaway, 1954); and Doll (1955) wrote: "We need to know . . . why the association which appears to exist between cancer of the larynx and cigarette smoking has not been reflected in an increase in the incidence of cancer of the larynx comparable to that believed to have occurred with cancer of the lung."

In almost 400 edematous fibromas of the vocal cord, none has been known to undergo cancerous changes (Myerson, 1955a).

In a study of 4,580 individuals made by Ogden (1955), 7.3% of smokers complained of frequent coughs, compared to 2.6% of non-smokers; in this series, 60.2% of the men smoked and 26.4% of the women.

In a series of 100 consecutive cases of carcinoma of the larynx, the lesion occurred 3.5 times more often in those who smoked a pack or more of cigarettes a day than in non-smokers (Woodward, 1955).

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

In the department of Antioquia, Colombia, Correa (1955) found 32 cases of cancer of the larynx in males and 17 in females, and he thought this large number of laryngeal-cancer cases in women might be related to the fact that, in Antioquia, many women smoke heavily and inhale the smoke. In some cases, the lesion has been found associated with the habit of smoking small cigars with the lighted end inserted into the mouth.

On the basis of tests on 18 physicians, Fishbein (1955) reported that changing to filter-tip cigarettes for 2 months resulted in a decrease in the amount of mucus in the throat and an accompanying disappearance of cough in most instances, and similar results were said to have been obtained on 24 other persons with cigarette cough.

One of the causes of elongation and hypertrophy of the uvula without acute inflammation may be the excessive use of tobacco over a long period of time (Kuyrkendall, 1955). Increased vascularity and firmness of the uvula has been observed in persons who have been smoking heavily for a long period of time (Myerson, 1955b). And, since smoking is said to influence the position and tone of the glossopharyngeal structures, excessive smoking was given as one of a large variety of conditions said to cause snoring (J. A. M. A. 144: 886, 1950).

Sanghvi, Rao and Khanolkar (1955) questioned 1460 patients who attended the cancer clinic of the Tata Memorial Hospital in Bombay during 1952-1954 concerning their tobacco habits. Results of the statistical analysis were said to show that the habit of chewing was associated with cancer of the oral cavity; that the combined habit of smoking and chewing was associated with cancer of the hypopharynx and base of the tongue; and that smoking only was associated with cancer of the oropharynx and esophagus. Patients referred to the cancer clinic for a check-up, but who showed no evidence of neoplastic disease, comprised the "control group."

Lickint (1956b) suggested that the lower incidence of laryngeal cancers *versus* lung cancer may perhaps be due not to a lack of carcinogenicity of the tobacco-smoke, but to the fact that the tar dust cannot deposit permanently in the laryngeal mucosa so easily as in the deeper respiratory passages, and also possibly to the fact that the laryngeal mucosa has a greater resistance to carcinogens than does the bronchial mucosa.

Thomson and Schaff (1956) reported 5 cases, all in cigarette-smokers, of carcinoma of the larynx with concurrent or subsequent development of bronchial carcinoma.

All of a group of 70 patients with cancer of the larynx used to excess some form of tobacco (Montreuil, 1956).

Studies undertaken at the Sloan-Kettering Institute during 1954-1956 have shown a direct relationship between the amount of tobacco smoked, either in cigarettes, pipes, or cigars, and the risk of developing cancer of the larynx (Rhoades, 1954-1956).

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

Wynder, Bross and Day (1956) made epidemiological surveys of cancer of the larynx in America and in India. The American results were based on 209 male patients with cancer of the larynx, contrasted to 209 matched controls and with 132 male patients with cancer of the lung. Patients with cancer of the larynx included significantly more smokers than the matched controls; there was only 1 laryngeal-cancer patient who was a non-smoker, compared to 22 among the controls. The Indian data were based on 132 patients with cancer of the extrinsic larynx and 132 matched controls; 2 of the cancer patients neither smoked nor chewed, compared to 18 among the controls. The risk of developing cancer of the larynx was found to increase with both bidi-smoking and betel-nut chewing, with the risk of the former being the greater.

Wynder (1956) considered the evidence as good that tobacco is a causative agent in cancer of the lung and larynx and hypopharynx and oral cavity, and as fair it is related to cancer of the esophagus, and suggestive, but without particular evidence, in cancer of the stomach.

The relative risk of developing cancer of the larynx was also said by Wynder, Bross and Day (1956) to increase with the amount of tobacco consumed.

Other factors said to be related to cancer of the larynx include: edentia, hoarseness, and chronic cough (Wynder, Bross and Day, 1956), and exposure to strong heat during performance of work (Blümlein, 1957).

Wynder and his associates (1956) have reported some evidence that alcohol consumption increases a smoker's susceptibility to laryngeal cancer [Study Group of Smoking and Health (1957)].

Rhoades (1954-1956) implied that tobacco-smoking was a "promoting" factor in the disease.

N. M. Kennaway and E. L. Kennaway (1936), analyzing the incidence of cancer of the larynx in England and Wales for 1921-1932, found that those occupied in supplying alcohol showed a much higher incidence of laryngeal than of lung cancer. It is not certain that the previously observed association of this disease with alcohol persists (Doll, 1954a). However, the influence of heavy alcohol consumption as one of the environmental factors in laryngeal cancer has been emphasized (Rhoades, 1954-1956; Wynder, Bross and Day, 1956; Fior, 1957).

Pemberton and Macleod (1956) reported a survey of 642 men over 40 years of age living or working in 6 of 16 towns in the Nashoba Health District of Massachusetts, in which 23.8% were found to be either non-smokers or ex-smokers; 72 of the smokers reported having smoker's cough. A survey of 1,274 men by A. M. Phillips, R. W. Phillips and Thompson (1956) revealed an incidence of 34% of chronic cough;

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According to the information Hilding (1956d) had been able to glean from laryngologists, it would seem that 80-85% of all of the carcinomas occurring in the larynx occur in the cords, and the majority of these occur on the anterior portion or right at the anterior commissure. Hilding related these findings to ciliary streaming, thus: If carcinogenic substances of whatever nature (including cigarette-tar), which have been inhaled and deposited on the mucous blanket of the respiratory tract cause cancer in the larynx, it would likely occur first where the application of the substance to the epithelium is longest and most intimate. Experiments on ciliary streaming in human larynges removed at autopsy indicated that that region would be at the anterior commissure of the anterior portion of the cords, where the mucous blanket comes to a standstill, divides, and passes backward along the two cords. Although Hilding felt it possible that the characteristics of the ciliary streaming in this area might account for the distribution of carcinomas, he added that it could not be so concluded from present evidence. Other factors also were to be considered, such as the impact of air on the upper surface of the cords, air eddies, as well as a comparatively large amount of mucus which is being discharged from the ventricle over the anterior portion of the cords. Further experiments made it a reasonable assumption to Hilding (1957a, b) that, at the vocal cords in the living person, the mucous blanket is torn asunder to flow in two opposite directions at right angles to the previous flow; and the author pointed out again that carcinomas are apt to occur upon the vocal cords where the squamous epithelium acts as an obstruction to flow.

Passey (1957) described changes in the mucous glands and goblet cells of the respiratory epithelium of rats exposed to cigarette-smoke, with a concomitant increase in free mucus in the trachea and bronchi; and he suggested that this might be a counterpart of the condition in man resulting in smoker's cough.

Landes and McCabe (1957) reported the case of a 38-year-old woman who presented a curious manifestation of dysphonia, presumably on an hysterical basis. Exposed to an atmosphere containing cigarette-smoke, her voice dropped sharply in pitch and assumed a raspy, hoarse quality; examination of her vocal cords showed them to be quite normal both before and during the periods of hoarseness. On exposure to non-smoke-laden air, the return of the voice to normal was almost instantaneous. On testing with pipe-smoke, no change whatever in the quality of the voice occurred.

W. C. Boake (reported in *Lancet*, Lond. 1: 512, 1957) confirmed the common impression that smokers coughed more, although they had no more sputum; they were said to have fewer sore throats, however—perhaps they had one all the time and did not notice it.

reference may be made to histological studies made by Michailow and Raitschew (1958) on the mucosa of the larynx of 100 smokers of both sexes in comparison with 10 non-smokers; the subjects were aged 40-70 years and had no indications of laryngeal disease. Smoking-related changes found were: thickening of the epithelium of the laryngeal mucosa; a more or less pronounced hyperkeratosis almost exclusively in the region of the true vocal cords; peculiarities of metaplasia of the cylindrical epithelium into a pavement epithelium. While these changes were not specific for tobacco, nevertheless the authors felt that they must be considered pre-carcinomatous if the individual has smoked cigarettes for a great number of years.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

Wynder and his associates (1957) studied a group of 265 males and 207 females with squamous-cell cancer of the upper alimentary and respiratory tracts, collected at the Radiumhemmet, Stockholm, in comparison with a control group of 115 males and 218 females with various other types of cancers at other sites; tobacco consumption of the patients was also analyzed. The data on women were said to show a relation between smoking and gum and buccal cancer, but smoking could not account for the relatively high frequency of cancer of the upper alimentary tract in Swedish women. Among the male patients, a significant relationship to smoking was found for cancer of the lip (in pipe-smokers), tongue (in cigar-smokers), upper hypopharynx (in cigarette-smokers), larynx (in cigarette- and cigar-smokers), and esophagus (in cigarette- and cigar-smokers). Tobacco-chewing was found to be of suggestive importance only in cases of cancer of the buccal mucosa and of the gingiva.

Following a statistical survey in the North Wales and Liverpool region, Stocks (1957) reported that female hospital patients with lung cancer in Liverpool showed a significant excess of smokers, compared to the controls; but those with stomach and breast cancer in rural North Wales and Liverpool did not differ from the controls in respect to past smoking history. In men, pipe-smoking, which increases the risk of lung cancer only slightly, was associated positively in the Liverpool and Lancashire areas with the incidence of cancers of the larynx, esophagus, intestine, and rectum, and in Cheshire and Denbigh S. E. with cancers of the larynx, esophagus, and intestine other than the rectum. The percentage of cigar- and pipe-smokers among male patients with cancer of the oral cavity was found by Wynder and Bross (1957) to be higher than in a control group of patients, and the relative risk for these was calculated to be higher than for cigarette-smokers. More of the cancer group chewed tobacco, compared to the controls, but the tobacco-chewers were also (with one exception) smokers.

Schwartz and Denoix (1957) found a statistically significant correlation between cigarette-smokers and pulmonary cancer and upper aero-alimentary cancer, but not other cancers; pipe-smokers were negatively correlated with pulmonary cancer, not correlated with upper aero-alimentary or other cancers. Schwartz, Denoix and Anguera (1957) further studied the possibility of an association between tobacco and cancers of all locations in 2147 cancer patients, each with a non-cancerous patient and disease-free patient as controls of the same age (within 5 years), questioned on the same date by the same investigator in the same group of hospitals. An association was observed with cancer of the lung, buccal cavity, oropharynx, hypopharynx, esophagus, and, probably, bladder. Locations belonging to the upper aero-alimentary tracts were divided into two groups: the group of the respiratory type (lung, larynx), in which the tendency to inhale smoke and the predominant use of cigarettes were particularly marked; and the group of the digestive-tract type (buccal cavity, pharynx, esophagus), where the smokers' habit of rolling their own cigarettes was particularly marked, at least in the case of the buccal cavity and esophagus.

Fior (1957) felt that there might be important extrinsic factors (e.g. smoking and drinking) which, by acting on the larynx, might enhance the hereditary cancer potential already existing in such subjects.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

In a series of 170 patients suffering from cancer of the larynx, 81.24% were said to have been exposed, during a very long period, to a continual action of the environmental factors of smoking and drinking (Fior, 1957). In a series of 102 histologically proved cases of cancer of the larynx, 100 were habitual smokers, almost exclusively of cigarettes; 2 had never smoked (Fusari, 1957). Pipe-smoking was associated positively in the Liverpool, Lancashire, Cheshire, and Denbigh S. E. areas with the incidence of cancer of the larynx (Stocks, 1957).

it has been suggested that smoking plays some part or role, or has some influence on the development of laryngeal cancer (Hoffman, 1931; Fior, 1957; Fusari, 1957); and a statistical association or relationship has been found by a number of recent workers (Sadowsky, Gilliam and Cornfield, 1953; Rhoades, 1954-1956; Schwartz, Denoix and Anguera, 1957; Stocks, 1957; Wynder *et al.*, 1957; Hammond and Horn, 1958b). Sitbon and Hadida (1953) have reviewed the literature on the role of tobacco in the development of laryngeal and broncho-pulmonary cancers. More recently, E. Kennaway (1957) reviewed some of the studies which have been made on the etiology of cancer of the larynx, particularly in connection with the role of tobacco; and he reflected on some of the questions they raise.

Blümlein (1958) concluded that only one noxa, namely, tobacco-tar inhaled with cigarette-smoke, can specifically explain the increasing incidence of laryngeal carcinoma within the framework of an increasing frequency of lung cancer.

In the still-continuing prospective study by Hammond and Horn (1958b), an extremely high association of cigarette-smoking with cancer of the larynx was evident.

In a series of 59 patients with cancer of the hypopharynx, 26% were heavy smokers (Barbosa, cited in J. A. M. A. 168: 802-803, 1958).

Sarma (1958) also reported a close correlation between the incidence of cancer of the larynx and the Assamese type of betel-nut-chewing habit; Assam is the easternmost state of India.

Wynder (1958) stated that in both laryngeal and oral-cavity cancer, the risk among cigar- and pipe-smokers of developing cancer in these regions was greater than their risk of developing lung cancer; and he presented data to indicate that, as one goes upward in the respiratory tract, the risk of developing cancer becomes greater for cigar- and pipe-smokers, while the cancer risk decreases for cigarette-smokers.

Wynder and co-workers (1958) also studied environmental factors in cancer of the respiratory tract in Cuba, based on 399 male and 107 female cases of cancer of the oral cavity, larynx, or lung, matched against controls. Whereas, in the male patients, 16% of the controls were non-smokers, only 1% of the laryngeal-cancer group were non-smokers; 42% of the larynx group admitted to smoking 35 cigarettes or the equivalent in cigars per day, in contrast to 29% for the controls. Cigarettes only were smoked by 49% of patients with cancer of the larynx; cigars only were smoked by 15% of the larynx group. In the females, there were 13% non-smokers in the larynx group, and 66% in the controls.

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EXTRACTED FROM LARSON, HAAG AND SILVETTE (1961)

Wynder and Lemon (1958) reported preliminary findings on differences in incidence of cancers between 564 Seventh-Day Adventists and 8128 others (i.e. non-Seventh-Day Adventists), the point of the comparison being that only 6% of the Seventh-Day Adventists had a smoking history of more than 20 years, which compares to 85.4% in a sample of the general population. Thus, the smoking habits of the Seventh-Day Adventists males are similar to those of females in the general population; in addition, for all practical purposes, Seventh-Day Adventists are a non-drinking population. Epidermoid cancer of the lung was found to be 10 times less common among Seventh-Day Adventists than among the general population; actually, there was only 1 lung-cancer case in a Seventh-Day Adventist, and cancers of the mouth, larynx, and esophagus (previously shown to be related not only to smoking, but also to heavy drinking) were at least 10 times less common among Seventh-Day Adventists men than among men of the general population. All other types of cancer, with the exception of cancer of the bladder and cervix, occurred with the same frequency as in the general population; the latter occurred slightly less often than in the general population. These data and conclusions have been reported more fully by Wynder, Lemon and Bross (1959).

an examination by Higgins (1957) of 331 men and 300 women, aged 25-74 years, in Wales showed that smokers of both sexes recorded a significantly higher prevalence of persistent cough and sputum than non-smokers; this was confirmed for Scotland and England (Higgins, 1958, 1959).

Analysis by Saslaw and Streitfeld (1959) of findings from 1812 throat swabbings showed that β -streptococci were isolated from the throats of present smokers almost twice as often as from non- or past smokers, a difference said to be statistically very significant ($p < 0.001$). Group A organisms were also isolated more frequently from smokers' throats, but this difference was not as statistically great ($p = < 0.05 > 0.02$). The higher frequency of streptococcal isolation among smokers than among non- and past smokers may be due to an effect of smoke products on streptococci or on the mucous-membrane barrier of the host. Antistreptolysin O studies (1611 samples) showed no appreciable difference in titers of sera from smokers compared to those from non-smokers.

According to Cracovaner (1959), hyperkeratotic lesions of the larynx are, in general, due to chronic irritation, among the sources of which is excessive smoking. Excessive smoking should be eliminated as part of the treatment of the condition.

Dutta-Choudhuri, Roy and Gupta (1959) ascertained tobacco habits in 582 patients with cancer of the larynx and hypopharynx, compared to those of 288 controls, from which they concluded that tobacco-smoking has a statistically significant role in the production of cancer of the larynx. Chewing tobacco did not similarly influence the incidence of cancer.

Stocks (1959) too stated that the risks of laryngeal cancer in men were increased in those who had been addicted to heavy cigarette-smoking.

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